



ORIGINAL RESEARCH PAPER

Anatomy

A STUDY ON HUMAN CADAVERIC PANCREAS: VARIATIONS IN DIAMETERS OF ISLETS OF LANGERHANS IN DIFFERENT AGE GROUP

KEY WORDS: Islets of Langerhans, Pancreas, different age group, variations in number

Baro Baneswar	Associate Professor, Department of Anatomy, Diphu Medical College, Diphu, Karbi Anglong, Assam, India
Rabha Gunamani	Assistant Professor, Department of Anatomy, Diphu Medical College, Diphu, Karbi Anglong, Assam, India
Sarma Usha	Professor, Department of Pathology, Gauhati Medical College, Guwahati, Assam, India
Talukdar KL	Principal, MGM Medical College and LSK Hospital, Kishanganj, India
Dutta BC	Principal, Lakhimpur Medical College, Lakhimpur, Assam, India
Sarma Tapan*	Associate Professor, Fakhruddin Ali Ahmed Medical College, Barpeta, Assam, India *Corresponding Author

ABSTRACT

INTRODUCTION: The islets of Langerhans may contain a few cells or many hundreds of polygonal cells arranged in short irregular cords that are abundantly invested with a network of fenestrated capillaries to produce a hormone with glucose-lowering effect. **MATERIALS AND METHODS:** The descriptive and cross-sectional study was done in the Department of Anatomy, Forensic Medicine & Pathology of Gauhati Medical College, Guwahati based on collection of 103 human pancreas aging from 13 to 78 years of both sexes. The collected samples were divided into group A (10-19 years), B (20-29 years), C (30-39 years), D (40-49 years), E (50-59 years), F (60-69 years) and G (≥ 70 years). Measurement of five slides selected from head, body and tail region were examined under 400 magnification. **RESULTS AND OBSERVATION:** The differences between the diameter of pancreatic islets for head part were statistically significant in A vs B, A vs D, A vs E, A vs F, A vs G, B vs D, B vs E, B vs F, B vs G, C vs E, C vs F, C vs G, F vs G in body part A vs B, A vs C, A vs F, A vs G, B vs C, B vs D, B vs E, B vs F, B vs G, C vs G, D vs G, E vs G and F vs G. and in tail part between A vs B, A vs C, A vs D, A vs E, A vs F, A vs G, B vs C, B vs D, B vs E, B vs G, C vs E, C vs F, C vs G, D vs F, D vs G, E vs F, E vs G and F vs G region. **CONCLUSIONS:** In the 3 region it was found that in the both extremities of life the diameter of islets of Langerhans was gradually decreased as age increases. Larger samples and advanced procedures in case of normal and abnormal population like people with diabetes disease for further studies may recommended.

INTRODUCTION

The islets of Langerhans, named after the German pathologist Paul Langerhans, constitute a critical organ unique in that it is split into about a million units hidden in the pancreas, thus contributing to the enormous difficulty in harvesting them. French histologist Edouard Laguesse was suggested that the structures constituted the endocrine part of the pancreas with a possibility to produce a hormone with glucose-lowering effect.¹

It is unclear why nature has chosen to locate islets in the pancreas. The location is however advantageous, since the hormones are secreted directly into the portal vein enabling direct control of the hepatic function. Furthermore, it is speculated that a vascular system that allows the exocrine pancreas tissue to be nourished by endocrine hormones may have had importance during some stages of evolution explaining location of islets amidst the acinar lobules.²

Islets of Langerhans arise from gut tube endoderm.³ Each islet is surrounded by a collagen capsule. Characterization of different collagens in the islet-exocrine interface shows that collagen I, IV, V and VI are present and that collagen VI is the major component in the extracellular matrix.⁴

Being a mixed gland, the pancreas consists of two distinct populations of cells, the exocrine cells constituting 98% of the gland secrete enzymes into the digestive tract, and the endocrine cells 2% of the glandular mass that secrete hormones into the bloodstream.⁵ The endocrine pancreas is a diffuse organ scattered as small nest of cells called islets of Langerhans which is usually numerous in tail region of the pancreas.⁶ Pancreatic islets may contain a few cells or many hundreds of polygonal cells arranged in short irregular cords

that are profusely invested with a network of fenestrated capillaries.⁷

In haematoxylin and eosin (H & E) stained sections, the islets of Langerhans appear as cluster of pale staining cells surrounded by more intensely staining pancreatic acini.^{7,8} The pancreatic islet function is closely associated with the morphologic changes in islet cells.⁹ The most common disease of the endocrine pancreas is diabetes mellitus associated with changes in the size and number of islets.^{10,11} Moreover, male population predominantly suffers from diabetes mellitus.¹² The most promising research for diabetes mellitus is in producing stem cells where researchers are looking to make possible for diabetics to have a new pancreas.¹¹ Recently, islet cells were successfully generated in vitro from human pancreatic stem cells.¹³ However, sufficient investigation has not been made into how many islets are contained in a unit volume of pancreas, or how differently they behave in their size distribution and still there are scopes to gain insight into their functional relationships and changes in disease process.¹⁴

Scientists have made many advances in islet transplantation in recent years. However, most recipients returned to using insulin because the transplanted islets lost their ability to function over time. Besides, the researchers also noted that many transplant recipients were able to reduce their need for insulin, achieve better glucose stability, and reduce problems with hypoglycaemia.¹⁵ Another important point is that large amounts and excellent viabilities of pancreatic islets are prerequisites for recent advances in islet transplantation. Cryopreservation has been shown to enlarge transplanted cell mass, but has been accompanied by reduced viability, where a negative correlation between islet size and viability

observed in non-frozen islets¹⁶. Post mortem examination of the pancreas in long-term diabetes shows an absence or greatly reduced number of insulin-staining beta cells; the residual pseudoatrophic islets contain abundant alpha cells and show light fibrosis¹⁷.

Literature on study on pancreas in terms of histology and morbid anatomy is not available from this part of the country (North East India). This study was done considering the seriousness of pancreatic diseases and the utmost importance of its correct diagnosis and treatment.

MATERIALS AND METHODS:

This descriptive and cross-sectional study was done in the Department of Anatomy, Forensic Medicine & Pathology of Gauhati Medical College, Guwahati from May, 2016 to December, 2019, based on collection of 103 human pancreas aging from 13 to 78 years of both sexes, excluding any apparent signs of putrefaction of the viscera, any injury in pancreas, death due to poisoning, known pancreatic disease and specimens having medicolegal obligation. Simple random samplings were used for sampling method.

The collected samples were divided into seven age groups: A (10-19 years), B (20-29 years), C (30-39 years), D (40-49 years), E (50-59 years), F (60-69 years) and G (≥ 70 years), for convenient description of their various age-related changes (according to Varley et al.)¹⁸.

Preparation of the slides: Selection of the tissue were cut (3 mm x 3 mm) with scissors for histological study. The length of the tissue was 1 inch. The histological slides were prepared by using standard procedure with Harris's Haematoxylin and Eosin (H & E) stain.

Measurement of average diameter of islets of Langerhans: For measurement of diameter of islets of Langerhans, five slides were selected from head, body and tail region were examined under 400 magnification ($\times 40$ objectives, $\times 10$ eyepiece). The diameter of islets of Langerhans was measured by using a stage micrometer and ocular micrometer. Micrometry was done following Drury R.A.B et al¹⁹. Two measurements were taken for each of islets of Langerhans. One measurement was taken at the maximum transverse diameter of islets and the other was perpendicular to the previous one. Hence, the transversal diameter of the islets of pancreas was measured by taking the mean of the two diameters as follows:

$$\text{Average diameter} = (\text{Maximum transverse diameter} + \text{Maximum perpendicular diameter}) \div 2$$

The stage micrometer calibration was focused under 40x objective and the 10x ocular micrometer calibration was super imposed on them in such a way that the starting mark on the ocular micrometer matches exactly with the starting mark on the stage micrometer. Then the marker on the stage and ocular micrometer that corresponds to each other most closely was noted. In this way, determination of how many of the smallest division of the ocular micrometer corresponded with how many of the smallest division of the stage micrometer was done. Then the calculation was done to determine the average diameter of the islets of pancreas

Statistical processing of data: Data were collected and appropriate statistical analyses were done by using IBM SPSS version 26. Paired sample t-test was conducted to check for significant difference in the average number of islets in head, body and tail. A p-value of less than 0.05 indicates significant difference in the average number of islets between two groups.

Ethical clearance: The study was approved by the Institutional Ethics Committee of Gauhati Medical College, Guwahati. A written informed consent had been taken in

English as well as in Assamese languages from the attendants and permission from concerned authority for post mortem cases.

RESULTS AND OBSERVATION:

Diameter of Islets of Langerhans in the head of the pancreas: The average diameter of pancreatic islets were found $106.00 \pm 1.15\mu\text{m}$, $103.68 \pm 0.85\mu\text{m}$, $100.88 \pm 9.64\mu\text{m}$, $89.66 \pm 12.16\mu\text{m}$, $84.08 \pm 4.63\mu\text{m}$, $88.40 \pm 0.64\mu\text{m}$ and $79.16 \pm 2.11\mu\text{m}$ in group A, B, C, D, E, F and G respectively. The differences between the diameter of pancreatic islets were statistically significant in A vs B, A vs D, A vs E, A vs F, A vs G, B vs D, B vs E, B vs F, B vs G, C vs E, C vs F, C vs G, F vs G (table 9). In the present study, the diameter of Islets of Langerhans were decreased up to E group and again increased in F group before decreased in G group. In the head region the diameter was gradually decreased as age increases.

Diameter of Islets of Langerhans in the body of the pancreas: The average diameter of pancreatic islets were found $80.48 \pm 1.10\mu\text{m}$, $110.34 \pm 0.83\mu\text{m}$, $94.42 \pm 9.81\mu\text{m}$, $83.44 \pm 5.35\mu\text{m}$, $83.20 \pm 4.74\mu\text{m}$, $84.62 \pm 1.15\mu\text{m}$ and $76.72 \pm 1.69\mu\text{m}$ in group A, B, C, D, E, F and G respectively. The differences between the diameter of pancreatic islets were statistically significant in A vs B, A vs C, A vs F, A vs G, B vs C, B vs D, B vs E, B vs F, B vs G, C vs G, D vs G, E vs G and F vs G (table 9). In the present study, the diameter of Islets of Langerhans was found to be increased in group B, then gradually it decreased in diameter. The decreased diameter in the body part was found in the both extremities of life.

Diameter of Islets of Langerhans in the tail of the pancreas: The average diameter of pancreatic islets were found $81.92 \pm 0.70\mu\text{m}$, $100.22 \pm 1.13\mu\text{m}$, $115.0 \pm 10.51\mu\text{m}$, $122.84 \pm 6.18\mu\text{m}$, $132.16 \pm 5.61\mu\text{m}$, $99.12 \pm 0.40\mu\text{m}$ and $96.30 \pm 1.31\mu\text{m}$ in group A, B, C, D, E, F and G respectively. The differences between the diameter of pancreatic islets were statistically significant in A vs B, A vs C, A vs D, A vs E, A vs F, A vs G, B vs C, B vs D, B vs E, B vs G, C vs E, C vs F, C vs G, D vs F, D vs G, E vs F, E vs G and F vs G (table 9). In the present study, the diameter of Islets of Langerhans increased up to group E then gradually it was decreased. The decreased diameter in the tail part of pancreas was found in the both extremities of life.

TABLE - 1 ANALYSIS REPORT OF DIAMETER OF ISLETS OF LANGERHANS IN THE HEAD, BODY AND TAIL OF THE PANCREAS IN GROUP A (10 to 19 Years):

Slide No	Head	Body	Tail
1	107.3	79	80.8
2	106.3	81.4	82.8
3	104.3	79.6	82.2
4	105.5	81.1	82.3
5	106.6	81.3	81.5
Sum	530	402.4	409.6
Mean	106	80.48	81.92
SD	1.15	1.10	0.70

TABLE - 2 ANALYSIS REPORT OF DIAMETER OF ISLETS OF LANGERHANS IN THE HEAD, BODY AND TAIL OF THE PANCREAS IN GROUP B (20 to 29 Years):

Slide No	Head	Body	Tail
1	103.2	110.1	98.7
2	104.6	111.8	99.8
3	103.1	110	101.3
4	104.6	110.1	101.4
5	102.9	109.7	99.9
Sum	518.4	551.7	501.1
Mean	103.68	110.34	100.22
SD	0.85	0.83	1.13

TABLE – 3 ANALYSIS REPORT OF DIAMETER OF ISLETS OF LANGERHANS IN THE HEAD, BODY AND TAIL OF THE PANCREAS IN GROUP C (30 to 39 Years):

Slide No	Head	Body	Tail
1	107.2	111.2	126.9
2	104	94.9	113.5
3	86.3	87	98.5
4	110.4	89.4	119.9
5	96.5	89.6	116.2
Sum	504.4	472.1	575
Mean	100.88	94.42	115
SD	9.64	9.81	10.51

TABLE – 4 ANALYSIS REPORT OF DIAMETER OF ISLETS OF LANGERHANS IN THE HEAD, BODY AND TAIL OF THE PANCREAS IN GROUP D (40 to 49 Years):

Slide No	Head	Body	Tail
1	106.9	78.2	127
2	97.7	86.5	128.4
3	80.4	82.1	117
4	84.4	79.3	126.5
5	78.9	91.1	115.3
Sum	448.3	417.2	614.2
Mean	89.66	83.44	122.84
SD	12.16	5.35	6.18

TABLE – 5 ANALYSIS REPORT OF DIAMETER OF ISLETS OF LANGERHANS IN THE HEAD, BODY AND TAIL OF THE PANCREAS IN GROUP E (50 to 59 Years):

Slide No	Head	Body	Tail
1	89.8	89	139.6
2	80	84.7	132.2
3	84	76.1	128.3
4	87.5	84.4	125.4
5	79.1	81.8	135.3
Sum	420.4	416	660.8
Mean	84.08	83.2	132.16
SD	4.63	4.74	5.61

TABLE – 6 ANALYSIS REPORT OF DIAMETER OF ISLETS OF LANGERHANS IN THE HEAD, BODY AND TAIL OF THE PANCREAS IN GROUP F (60 to 69 Years):

Slide No	Head	Body	Tail
1	87.5	84	98.9
2	88.6	84.9	99.1
3	88.6	83.2	99.4
4	89.2	86.3	99.6
5	88.1	84.7	98.6
Sum	442	423.1	495.6
Mean	88.4	84.62	99.12
SD	0.64	1.15	0.40

TABLE – 7 ANALYSIS REPORT OF DIAMETER OF ISLETS OF LANGERHANS IN THE HEAD, BODY AND TAIL OF THE PANCREAS IN GROUP G (≥70 Years):

Slide No	Head	Body	Tail
1	77.4	74	98
2	82.3	76.3	96
3	77.3	77.4	97.3
4	80.2	78.4	95.2
5	78.6	77.5	95
Sum	395.8	383.6	481.5
Mean	79.16	76.72	96.3
SD	2.11	1.69	1.31

TABLE – 8 DIAMETER OF ISLETS OF LANGERHANS IN THE HEAD, BODY AND TAIL OF THE PANCREAS IN DIFFERENT AGE GROUP

Group (n)	Average diameter of islets of Langerhans(µm) =Mean± SD(Range)		
	Head Mean±SD	Body Mean±SD	Tail Mean±SD
A (5)	106.00 ±1.15(104.3 – 107.3)	80.48 ± 1.10 (79.0 – 81.4)	81.92± 0.70 (80.8 – 82.8)
B (5)	103.68± 0.85 (102.9 – 104.6)	110.34 ± 0.83 (109.7 – 111.8)	100.22± 1.13 (98.7 – 101.4)
C (5)	100.88 ± 9.64 (86.3 – 110.4)	94.42 ± 9.81 (87.0 – 111.2)	115.0± 10.51 (98.5 – 126.9)
D (5)	89.66 ± 12.16 (78.9 – 106.9)	83.44 ± 5.35 (78.2 – 91.1)	122.84± 6.18 (115.3 – 128.4)
E (5)	84.08 ± 4.63 (79.1 – 89.8)	83.20 ± 4.74 (76.1 – 89.0)	132.16 ± 5.61 (125.4 – 139.6)
F (5)	88.40 ± 0.64 (87.5 – 89.2)	84.62 ± 1.15 (83.2 – 86.3)	99.12 ± 0.40 (98.6 – 99.6)
G (5)	79.16 ± 2.11 (77.3 – 82.3)	76.72 ± 1.69 (74.0 – 78.4)	96.30 ± 1.31 (95.0 – 98.0)

TABLE – 9 NUMBER OF ISLETS OF LANGERHANS IN THE HEAD, BODY AND TAIL OF THE PANCREAS IN DIFFERENT AGE GROUP

Comparisons of groups	p-Value in the different parts of pancreas		
	Head p-Value	Body p-Value	Tail p-Value
A vs B	0.007	<0.001	<0.001
A vs C	0.272	0.013	<0.001
A vs D	0.017	0.260	<0.001
A vs E	<0.001	0.247	<0.001
A vs F	<0.001	<0.001	<0.001
A vs G	<0.001	0.003	<0.001
B vs C	0.536	0.007	0.014
B vs D	0.033	<0.001	<0.001
B vs E	<0.001	<0.001	<0.001
B vs F	<0.001	<0.001	0.074
B vs G	<0.001	<0.001	<0.001
C vs D	0.145	0.059	0.188
C vs E	0.008	0.05	0.012
C vs F	0.020	0.057	0.01
C vs G	0.001	0.004	0.004
D vs E	0.366	0.942	0.037
D vs F	0.823	0.643	<0.001
D vs G	0.094	0.028	<0.001
E vs F	0.073	0.533	<0.001
E vs G	0.063	0.021	<0.001
F vs G	<0.001	<0.001	0.002

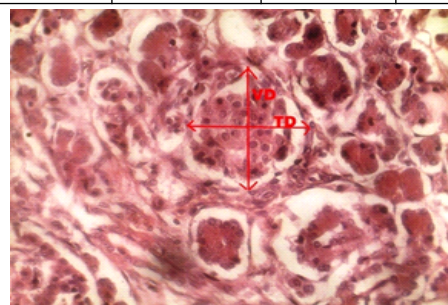


Figure 1: Showing Islets of Langerhans (400X magnification) (VD=Vertical Diameter, TD= Transverse Diameter)

DISCUSSION

According to Iki K¹⁷, in humans islets of Langerhans constitute spherical or ellipsoid clusters of cells with a diameter

between ~50-250 µm. Some islets in diabetics can be very large, up to ~350 µm in diameter, because of oedema and deposition of amyloid. Hellman B.²⁰ mentioned that the number of islets in a given pancreas increases with a decreasing diameter of the islets. Most of the islets in the pancreas are of small diameter, i.e., ~50-100 µm. However, medium sized islets with a diameter of ~100-200 µm contribute most to the total islet volume at all ages with the only exception of the newborn, where it is the opposite. Hellman B.^{20,21} mentioned that number of islets increases progressively with decreasing diameter where highest diameter does not exceed 300µ and in hyaline changes islets were about 400µ diameter. K. Saito et al.²² found the mean radius of islets were .0133±.0036 and .0206±.0057 in the head and tail region respectively. The study of Ionescu-Tirgoviste et al.²³ revealed that the human pancreas the mean islet diameter is 108.92 µm (±6.27 µm),

Constantin IT et al.²⁴ found the mean of total area(mm²) were 0.578±.467, 0.875±0.391 and 0.887±0.633 in the head, body and neck part respectively. Soejima & Landing²⁵ found that the pancreatic islets in diabetes showed hypertrophy, where the mean volume/ diameter of the three largest pancreatic islets was 0.00795±0.00599 mm, being larger than the normal. Mescher²⁶ stated that the diameter of the islets ranges from 100 to 200 µm, which is in agreement with the present study.

In the study of Shahriah S et al.²⁷, the diameter of islets of Langerhans was found to be gradually increased with advancing of age up to 49 years, then decreases again. However, the number of cells and extent of diameter of islets were within the range described by Murtaugh & Melton²⁸.

CONCLUSIONS

In the head, body and tail region it was found that in the both extremities of life the diameter of Islets of Langerhans was gradually decreased as age increases.

The diameter of Islets of Langerhans in the head part were decreased, but in the tail part it was increased up to 50-59 years group. In the body part it was increased upto 20-29 years. Larger samples and advanced procedures in case of normal and abnormal population like people with diabetes disease for further studies may recommended.

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